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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/909,012	07/19/2001	Anil K. Saksena	IN01158K	8726

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SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER

MONDESI, ROBERT B

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/909,012	Applicant(s) SAKSENA ET AL.	
	Examiner Robert B Mondesi	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20,25-31 and 38-40 is/are pending in the application.
- 4a) Of the above claim(s) 2,6,30,31,39 and 40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-5,7-20,25-29 and 38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This office action is in response to amendment filed March 23, 2004. **Claims 1, 3-5, 7-20, 25-29 and 38** (with a further election of a "core structure" represented by the third compound in claim 25 on page 178) as drawn to elected Invention I are currently pending and are under examination. **Claims 21-24 and 32-37** have been cancelled. **Claims 2, 6, 30-31 and 39-40** are withdrawn for being drawn to non-elected subject matter. **Claims 1, 3-5, 7-20, 25-29 and 38** are currently under examination.

Withdrawal of Objections and Rejections

The rejection of **claims 3, 19, 25, 26 and 28** under 35 U.S.C § 112, second paragraph is withdrawn.

The rejection of **claim 19** under 35 U.S.C § 101 as being drawn to non-statutory subject matter is withdrawn.

The rejection of **claim 1** under 35 U.S.C § 102(b) as being anticipated by McIver et al. is withdrawn.

New Rejection(s) and Objection(s)

Specification

The disclosure is objected to because of the following informalities: There are gaps and blank segments on the following pages of the specification: pages 43, 50, 54,

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96, and 130. The presence of such gaps and blank segments suggests the possibility of missing text. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-25, 27 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for, compounds in tables 1-4 (compounds 1-133, pages 26-29, 136-159) does not reasonably provide enablement for all the compounds presented by the general structure formula (I) of claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use or make the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized in *re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir.1988). The court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed

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invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the relative skill of those in the art, (5) the predictability or unpredictability of the art, (6) the amount or direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In Wands, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (Wands, 8 USPQ2d 1406). Thus, a combination of factors which, when viewed together, would provide an artisan

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of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of Wands factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

1. Breadth of the claims.

In regards to the method of the invention and the breadth of the claims the broadest interpretation that applies is to compounds presented by the general structure formula (I) of claim 1.

2. The nature of the invention.

The invention is a novel class of pharmaceutical compounds that are inhibitors of Hepatitis C Virus (HCV) protease activity, specifically compounds that inhibit HCV NS3/NS4a serine protease activity.

3. The state of prior art.

In regards to the compounds of the invention presented by the general structure formula (I) of claim 1, the prior art does not provide any evidence of HCV protease inhibitory activity- specifically with regards to HCV NS3/NS4a serine protease inhibitory activity.

4. The relative skill in the art.

The relative skill in the art as it relates to pharmaceutical compounds that inhibit the activity of HCV serine protease is that of a M.D. or Ph. D. level individual.

5. The level of predictability in the art.

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Since the prior art does not teach that the compounds presented by general formula (I) of claim 1 formerly existed, the level of predictability is low in regards to the compounds of the invention with respect to HCV serine protease inhibitory activity. Therefore, one of skill in the art would not be able to readily anticipate the inhibitory effects of the compounds of the invention in view of HCV NS3/NS4a serine protease inhibitory activity.

6. The amount of guidance present.

The applicants have not provided guidance for all the compounds presented in the general formula (I) of claim 1. In table 1 (pages 26-29) of the specification of the present application, the applicants have provided results of a HCV protease continuous assay for a group of compounds wherein the applicants have categorized the K_i values associated with each investigated compound as a barometer of HCV serine protease inhibitory activity. If the K_i of a given compound is between 1-100 nM then the compound is in category A, If the K_i of a given compound is between 101-1000 nM then the compound is in category B, any value for a given compound that is above 1000nM is considered to be in category C. It is obvious to a person skill in the art that there is wide range of K_i values that is associated with these compounds, for example compound 25 has a K_i value that is between 1-100 nM whereas compound 10 has K_i value that is above 1000 nM. With such an apparent wide range of HCV protease activity it is pertinent that the applicants disclose further experimentation to show to a person skill in the art the level of potency for a given compound of the invention. Such information is required by a person skill in the art in order to be able to use the correct

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amount of the compound of the invention in a process such as an assay or a method of treatment. Furthermore the applicant has only shown how to make a limited number of the peptides of the invention, compounds 1-133 (examples 1-20), since the general structure formula of claim 1 allows for a much larger number of possible peptides than disclosed, a person skill in the art would need more guidance as to how to make all the compounds presented by the general structure formula of claim 1. In view of the compounds of the invention, the applicants have shown some guidance as to how compounds of the invention, compounds in tables 1-4 (compounds 1-133, pages 26-29, 136-159) and in the specification examples 1-20 (Pages 46-91) can be made and perhaps used to inhibit HCV protease activity - but the applicants have not provided guidance, for all the compounds presented in the general structure formula (I) of claim 1 in, regards to how they can be made and used to inhibit HCV serine protease activity.

7. The existence of working examples.

The specification, examples 1-20 (Pages 46-91) provides specific working examples of compounds in tables 1-4 (compounds 1-133, pages 26-29, 136-159) that can be used to inhibit HCV serine protease activity. However, the specification does not provide working examples of all compounds suggested by the general structure formula (I) of claim 1.

8. The quantity of experimentation necessary.

In the case of using all the compounds suggested by the general structure formula (I) of claim 1, a large quantity of experimentation would be required in order for a person skill in the art to be able to practice the invention, since there are a multitude of

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possible compounds that are suggested by the general structure formula of claim 1 and each compound needs to be tested for HCV protease inhibitory activity.

Due to the quantity of experimentation still required to be performed by one skill in the art in regards to how to use all the compounds suggested by the general formula (I) of claim 1, the lack of guidance presented in the specification regarding the same, the absence of a working example directed to same, the unpredictable nature of the invention with regards to HCV serine protease inhibitory activity of each compound, the state of the prior art not providing any evidence that all the compounds suggested by general formula (I) of claim 1 will exhibit HCV serine protease inhibitory activity, and the breath of the claims which fails to provide particular steps for all compounds suggested by the general formula (I) of claim 1 exhibiting HCV serine protease inhibitory activity, the specification fails to teach the skilled artisan in the art how to make and use the invention.

Conclusion

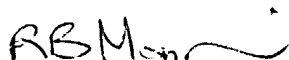
No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

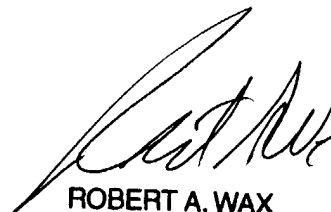
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Robert B. Mondesi
Patent Examiner
Group 1653

05-14-03


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PRIMARY EXAMINER